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IT IS CLAIMED:

1. A method of identifying one or more of a plurality of different sequences in a target polynucleotide,
5 comprising

adding to the target polynucleotide, a plurality of sequence-specific probes, each characterized by (a) a binding polymer having a probe-specific sequence of subunits designed for base-specific binding of the binding 10 polymer to a target sequence, under selected binding conditions, and (b) attached to the binding polymer, a polymer chain having a ratio of charge/translational frictional drag which is different from that of the binding polymer,

15 reacting the probes with the target polynucleotide under conditions favoring binding of the probes in a base-specific manner to the target polynucleotide,

treating the probes to selectively modify those probes which are bound to the target polynucleotide in a sequence-specific manner, to form modified, labeled probes 20 characterized by (a) a distinctive ratio of charge/translational frictional drag, and (b) a detectable reporter label, and

fractionating the modified, labeled probe(s) by 25 electrophoresis in a non-sieving medium.

2. The method of claim 1, wherein the probe binding polymers are oligonucleotides.

30 3. The method of claim 1, wherein the different-sequence binding polymers have substantially the same lengths.

4. The method of claim 1, wherein said fractionating 35 is carried out by capillary electrophoresis.

5. The method of claim 1, wherein (i) each sequence-specific probe includes first and second probe elements having first and second oligonucleotides effective to bind 5 to adjacent regions of a target sequence, where one of the oligonucleotides is derivatized with said polymer chain, (ii) said reacting is effective to bind both oligonucleotides to its specific target sequence, (iii) said treating includes ligating the oligonucleotides bound 10 to the target polynucleotide under conditions which are effective to ligate the end subunits of target-bound oligonucleotides when their end subunits are base-paired with adjacent target bases, to form the ligated probes, and releasing the ligated probe from the target polynucleotide, 15 and (iv) the polymer chain attached to each different-sequence first oligonucleotide is effective to impart to the modified, labeled probe, a distinctive ratio of charge/translational frictional drag.

20 6. The method of claim 5, wherein the second probe element is reporter labeled, and said ligating is carried out with ligase enzyme.

7. The method of claim 5, wherein said treating 25 further includes subjecting the ligated probe to repeated cycles of probe binding and ligation, to amplify the concentration of ligated probe.

8. The method of claim 5, wherein said treating 30 includes subjecting each ligated probe to repeated cycles of probe binding and ligation in the presence of a second pair of probe elements having oligonucleotides which, together, make up a sequence which is complementary to the selected ligated probe, to amplify the ligated probe in a 35 geometric manner.

9. The method of claim 5, wherein said second probe element in each probe pair includes two alternative-sequence oligonucleotides which (i) are complementary to 5 alternative sequences in the same portion of the associated target region and (ii) are derivatized with different detectable reporters, and said detecting includes determining the sequence of each of said regions according to (a) a signature electrophoretic migration rate of each 10 probe, which identifies the target region associated with that probe, and (b) a signature reporter moiety, which identifies the mutation state of that region.

10. The method of claim 1, wherein (i) each sequence-specific probe includes first and second primer elements 15 having first and second sequence-specific oligonucleotides effective to hybridize with opposite end regions of complementary strands of a target polynucleotide segments, respectively, where the oligonucleotide in the first primer 20 element is derivatized with such probe-specific selected-polymer chain, (ii) said reacting is effective to bind both primer oligonucleotides to opposite end regions on complementary strands of the target polynucleotide, (iii) said treating is effective to amplifying the target segment 25 by primer-initiated polymerase chain reaction, and (iv) the polymer chain attached to each different-sequence first oligonucleotide is effective to impart to the amplified target sequences, a distinctive ratio of charge/translational frictional drag.

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11. The method of claim 10, wherein the oligonucleotide in the second primer element is reporter labeled, and the labeled probes are double stranded polynucleotide fragments.

12. The method of claim 10, wherein said treating further includes hybridizing to the amplified target sequences, with such in single-stranded form, single-stranded, reporter-labeled oligonucleotides whose sequences 5 are complementary to regions of the amplified target sequences, to form labeled probes.

13. The method of claim 2, wherein each sequence-specific probe includes a binding polymer and an attached 10 reporter label, the polymer chain associated with each different-sequence probe imparts to that probe, a distinctive ratio of charge/translational frictional drag, and said treating includes reacting the hybridized probes and target with DNA polymerase in the presence of a 15 reporter-labeled nucleoside triphosphate molecule, to form said labeled probes.

14. The method of claim 2, wherein each sequence-specific probe includes a binding polymer composed of a 20 first single-stranded DNA segment, and a second segment which includes single-stranded RNA, the polymer chain attached to said first segment, and a reporter attached to said second segment, and said treating includes reacting hybridized probe with an RNase enzyme specific for RNA/DNA 25 substrate, to form modified, labeled probe lacking the polymer chain.

15. The method of claim 2, wherein each sequence-specific probe includes a binding polymer composed of a 30 first single-stranded DNA segment, and a second segment which includes single-stranded RNA, the polymer chain and reporter label are attached to said first segment, and said treating includes reacting hybridized probe with an RNase enzyme specific for RNA/DNA substrate, to form modified, 35 labeled probe lacking said second binding polymer segment.

16. The method of claim 2, wherein each sequence-specific probe includes an oligonucleotide binding polymer having a 5' end, said polymer chain and a reporter label are attached to an oligonucleotide subunit adjacent said 5' end, and said treating includes enzymatically cleaving said adjacent subunit from the binding polymer, forming a labeled probe whose polymer chain imparts to the probe, a distinctive charge/translational frictional drag.

10 17. The method of claim 1, wherein each sequence-specific probe includes a binding polymer and an attached reporter label, the polymer chain associated with each different-sequence probe imparts to that probe, a distinctive ratio of charge/translational frictional drag, 15 and said treating includes immobilizing said target polynucleotide, washing the immobilized target polynucleotide to remove probes not bound to the target polynucleotide in a sequence-specific manner, and denaturing the target polynucleotide to release probes 20 bound in a sequence-specific manner.

18. A probe composition for use in detecting one or more of a plurality of different sequences in a target polynucleotide, comprising
25 a plurality of sequence-specific probes, each characterized by (a) a binding polymer having a probe-specific sequence of subunits designed for base-specific binding of the polymer to one of the target sequences, under selected binding conditions, and (b) attached to the 30 binding polymer, a polymer chain which has a ratio of charge/translational frictional drag which is different from that of the binding polymer.

19. The composition of claim 18, wherein said polymer 35 chain is selected from the group consisting of polyethylene

oxide, polyglycolic acid, polylactic acid, polypeptide, oligosaccharide, and polyurethane, polyamide, polysulfonamide, polysulfoxide, and block copolymers thereof, including polymers composed of units of multiple 5 subunits linked by charged or uncharged linking groups.

20. The composition of claim 18, wherein each sequence specific probe further includes a second binding polymer having a reporter, where the first-mentioned and 10 second binding polymers in a sequence-specific probe are effective to bind in a base-specific manner to adjacent and contiguous regions of a selected target sequence, allowing ligation of the two binding polymers when bound to the target sequence in a sequence-specific manner, and the 15 polymer chain attached to the first binding polymer imparts to each ligated probe pair, a distinctive combined ratio of charge/translational frictional drag.

21. The composition of claim 18, wherein each 20 sequence specific probe further includes a second binding polymer, where the first-mentioned and second binding polymers in a sequence-specific probe are effective to bind in a base-specific manner to opposite end regions of opposite strands of a selected duplex target sequence, 25 allowing primer initiated polymerization of the target region in each strand, and the polymer chain attached to the first binding polymer imparts to each polymerized region, a distinctive combined ratio of charge/translational frictional drag.

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22. The composition of claim 18, wherein each probe includes a reporter label, and the polymer chain in each probe imparts to that probe, a distinctive ratio of charge/translational frictional drag.

23. The composition of claim 22, wherein the reporter label and polymer chain are both attached to a single subunit in the binding polymer.

5 24. The composition of claim 18, wherein each sequence-specific probe includes a binding polymer composed of a first single-stranded DNA segment, and a second segment which includes single-stranded RNA, a polymer chain attached to said first segment, and a reporter attached to 10 said second segment, and each polymer chain imparts to probe, a distinctive ratio of charge/translational frictional drag.